REMARKS

The Applicant expresses appreciation for the courtesies extended by Examiner Sean E. Aeder to Applicant's representative Lars Genieser during the telephonic interview on May 25, 2010 (herein, "Interview", summarized in the "Interview Summary" mailed May 28, 2010).

Applicant appreciates the Office Action of April 2, 2010 indicating on pages 2-3 that the spelling of the first inventor's name has been corrected, the objection to the specification has been withdrawn, and the rejections under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 102(b) have been withdrawn.

Applicant respectfully requests reconsideration in light of the amendments above and the remarks that follow.

Claims 1, 5-10, and 16-28 are pending. Claims 6, 8, 10, and 16-19 are withdrawn. Claims 2-4 and 11-15 are canceled. Claims 1, 5, and 28 are amended. Support for amended claims 1, 5, and 28 is found, for example, in paragraphs [0005] and [0037]-[0038] of the specification as filed.

On pages 3-6, the Office Action rejects claims 1, 5, 7, 9, and 20-28 under 35 U.S.C. § 112, first paragraph as allegedly not compliant with the written description requirement. Applicant respectfully traverses for the following reasons.

Applicant submits that the terms "hormone refractory" and "androgen independent" are terms of art, and that in the context of prostate cancer, a person having ordinary skill in the art would understand the two terms to be equivalent. A human or animal suffering from prostate cancer can be subjected to "hormone therapy", a term of art. "Hormone therapy" refers to a course of therapy that lowers the level or reduces the effect of a hormone, for example, an androgen such as testosterone, through the administration of drugs that lower serum testosterone, drugs that act as competitive androgen receptor antagonists, and/or surgical castration. Although initially effective at blocking tumor growth, this hormone therapy eventually fails, in that cancer cells develop that proliferate despite the hormone therapy. This stage of prostate cancer is referred to by those having ordinary skill in the art as "androgen independent" or "hormone refractory" prostate cancer. The terms mean that despite the lowering of testosterone levels or blocking of the effect of testosterone through drugs or surgery, the prostate cancer cells

proliferate despite, that is, independently of or refractory or resistant to, such treatment. The terms originally derive from the context of medical treatment of complex organisms, such as humans or animals, rather than from the context of cellular biology experiments performed under carefully controlled conditions.

The terms "androgen independent" and "hormone refractory" do <u>not</u> have the meaning that cells do not proliferate even when an androgen or hormone is present. That is, a cell is considered to be "hormone refractory" when it continues to proliferate even though a hormone, e.g., testosterone, is reduced to a very low level. If an increased rate of proliferation is observed when the same cell is exposed to a higher level of the hormone, the cell is still considered to be hormone refractory. That is, the cell's behavior at reduced levels of hormone determines whether it is characterized as being "hormone refractory" (the cell's behavior at normal or elevated levels of the hormone does not govern the characterization).

As discussed in paragraph [00042] of the specification as filed, the inventors of the present application determined that there must be some binding of androgen ligand to androgen receptors in hormone refractory prostate cancer cells for cells to proliferate. For this reason, the last sentence of paragraph [00042] states that "the widely used term 'androgen-independent' may be a misleading description of HR prostate cancer." This is a critique of the descriptive value of the term, in that the inventors have found that the cells present in the stage of prostate cancer termed "androgen independent" by those of ordinary skill in the art in fact require a small amount of androgen to proliferate. Nevertheless, the suboptimal descriptive value of the term does not alter the fact that there is a distinct type of prostate cancer cell that does not respond to hormone therapy, is generally lethal, and is termed "androgen independent" by those of ordinary skill in the art.

The Applicant does, however, appreciate that although Applicant may use terms as they are commonly understood by those of ordinary skill in the art, there may be value in selecting a term whose meaning is clearer to laypeople than another term, even though the terms are understood to be equivalent by those of ordinary skill in the art. Therefore, Applicant has amended claim 1 to replace the term "androgen-independent" with "hormone refractory", amended claims 5 and 28 to replace the term "ligand-independent" with "ligand refractory", and amended claim 28 to replace the terms "androgen-independent" and "estrogen-independent" with

"androgen refractory" and "estrogen refractory", respectively. The term "refractory" has the meaning of "not responsive to treatment" (see the attached dictionary definition, "refractory", Webster's II: New Riverside University Dictionary, Houghton Mifflin (1988) p. 988) and thus harks back to the original observations in medical treatment from which the term derives. As such, the meaning of the term "hormone refractory" is clear: a disease state not responsive to hormone therapy in which hormone levels are decreased. Therefore, although a person having ordinary skill in the art would understand the terms "androgen independent" and "hormone refractory" in the context of prostate cancer to be equivalent and refer to a state of a prostate cancer that does not respond to hormone therapy and the cancer cells associated therewith, Applicant, at the Examiner's suggestion, has replaced claim terms using "independent" with terms using "refractory".

Applicant submits that paragraph [00037] of the specification as filed discloses engineered cells that meet the limitations of claims 1 and 5 of the present Application. Paragraph [00037] discloses "introduc[ing] an epitope-tagged wildtype AR [androgen receptor] cDNA by retrovirus infection into HS [hormone sensitive] LNCaP human prostate cancer cells" to make LNCaP-AR cells. This meets the requirement of claim 1 of a "mammalian prostate cancer cell express[ing] an exogenous wild type androgen receptor polynucleotide that encodes an androgen receptor polypeptide" and of claim 5 of a "mammalian cancer cell ... stably express[ing] an exogenous wild type polynucleotide that encodes a nuclear receptor protein or polypeptide" (the androgen receptor being a nuclear receptor protein). Paragraph [00037] continues by stating that "[a] three-fold increase in AR levels in LNCaP-AR cells mimics the expression difference observed." This meets the requirement of claim 1 that "[the] total polypeptide level of said androgen receptor polypeptide ... is at least two-fold higher than the endogenous level of androgen receptor ... polypeptide in a hormone-sensitive prostate cancer cell" and of claim 5 that "said increased level of mRNA in said selected mammalian cancer cell is at least two fold higher than the endogenous level of mRNA in said hormone-sensitive mammalian cancer cell," Paragraph [00037] notes that "LNCaP cells infected with the empty vector failed to grow in steroid-depleted, charcoal-stripped serum unless supplemented with 100 pM of the synthetic androgen, R1881," behavior characteristic of the hormone sensitive cell phenotype. By contrast, paragraph [00037] notes that "LNCaP-AR cells grew in at least 80%

lower concentrations of R1881 [and] were also resistant to bicalutamide," this behavior, continued proliferation at lowered hormone levels, being characteristic of the hormone refractory phenotype, as required by claim 1 ("growth of said mammalian prostate cancer cell [being] hormone refractory") and claim 5 ("growth of said selected mammalian cancer cell [being] nuclear receptor ligand refractory").

Paragraph [00011] presents the use of these cells by "contacting the compound to be tested with [the] mammalian prostate cancer cell ... and then comparing one or more characteristics of the mammalian prostate cancer cell ... with the same one or more characteristics of a control mammalian prostate cancer cell to which the compound has not been administered, wherein a difference in ... the one or more characteristics indicates that the compound has an effect on the mammalian prostate cancer cell." Paragraph [00012] discloses that these characteristics can be physiological characteristics. Paragraph [00016] discloses "treating a hormone refractory prostate cancer in a patient [by] administering to the patient an agent that decreases ... the biological function of the androgen receptor," and one of ordinary skill in the art would understand that such treatment necessarily constitutes contacting hormone refractory prostate cancer cells with the agent or compound. Paragraph [00028] relates that a drug may "inhibit ... tumor growth" of cancer cells, for example, hormone refractory prostate cancer cells. Thus, the written description, for example, paragraphs [00011]-[00012], [00016], [00028], and [00037], presents all limitations of claims 1 and 5. The experiment presented in paragraph [00037] conveys to one of ordinary skill in the art that the Applicant was in possession of the subject matter claimed in claims 1 and 5, a method using a cancer cell expressing an exogenous wild type androgen receptor polynucleotide and exhibiting hormone refractory growth.

Because the subject matter of claims 1 and 5 and the remaining claims, which are dependent therefrom, were presented in the written description of the specification as filed, and that one of ordinary skill in the art would therefore understand that the inventors had possession of the claimed invention at the time the application was filed, claims 1 and 5 as amended and claims 7, 9, and 20-28 dependent therefrom comply with 35 U.S.C. § 112, first paragraph. Applicant therefore respectfully requests that the rejection of claims 1, 5, 7, 9, and 20-28 be withdrawn.

Applicant hereby requests continued examination, and the Commissioner for Patents is authorized to charge the fee of \$405 due for a small entity for a Request for Continued Examination (RCE) to Deposit Account Number 22-0261, under Order Number 58086-232451. If any additional fee or any refund is deemed due, for this filing and any filing made hereafter by this firm for this Application, the Commissioner for Patents is authorized to charge the fee or credit the refund to Deposit Account Number 22-0261, under Order Number 58086-232451.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided. Applicant respectfully requests that a Notice of Allowance of all pending claims not withdrawn, claims 1. 5, 7, 9, and 20-28, be timely issued in this case.

Respectfully submitted,

Lars H. Genieser, Ph.D.

Registration No. 46,722 VENABLE LLP P.O. Box 34385

Washington, D.C. 20043-9998 Telephone (Direct): (202) 344-8234

Telephone (Main): (202) 344-4000

Telefax: (202) 344-8300

DC2/1109518

Date: July 2, 2010

to an authority for arbitration, decision, or examination, 5. To direct to an authority for arbitration, decision, or examination. 5. To direct the attention of —vil. 1. To persain concern <comments referring to the author's hat book > 2. To allude or make reference <comments to Virginia s the Cold Dominion > 3. To turn to, as for information or, authority. —refereable (refere-ble, Infelt') adj. —re-fere's Infelt') re-fere's infeltigation of authority. —refere's infeltigation of the comments of th

(Irfdirál) n. —re-ferrer n. referred, esp. for settlement of deficial value in a for settlement or decision. 2. An official supervising the play in a sport : UMFRE. 3. Lew. One appointed by a court to examine an report on a cust. —v. reed, reering, rees. —v. To judge as referred to the court of the customer of the

aport UMPRE. 8 Low. One appointed by a court to examine an extension of the court o

referent (ref'er-ont, ri-fur'ent) n. 1. Something that refers, esp. 2 linguistic item in its capacity of referring to a meaning 2. Something re-fill (rb-fil') vt. -filled, -fill-ing, -fills. To fill again. -n. (re-

re-till (tel-li) v. -filled, -fill-ling, -fills, To fill again. —a (tel-li). I. A product packaged or replace the used contents of a container. 2. A second or subsequent filling, re-filled (fiftin) v. -fined, -fined, -fines, -vv. 1. To reduce to a paire state: VARITE. 2. To remove by purifying, 3. To free from coarse characteristics. —vil. 1. To become free of impurities. 2. To acquire polish or elegance. 3. To use subslety and precise distinctions in thought or speech. —re-finiter a.

pouss or esgance. S. 10 use subtlety and precise distinctions in thought or speech. —re-fire'rs. n. re-fined (if-find') adl. I. Marked by good teste and broad knowledge as a result of development and education. Z. Free of imputities: INUSHED. S. Extremely precise.

* Symmal REPRING, CULTURED, URBANE, WELL-SRED

* \$7906 MENGED, CULTIVATED, CULTURED, URBANE, WALL-SEED add, commenting marked by good taste and bross knowledge as result of development and education < had refined, finishing-school manness/ antic course, crude refined ment (if.fir'mont) a. 1. An act of refining or the state of being refined. 2 The result of refining, as an improvement or calculation. 3. Pineness of thought or expression: CULTIVATION. 4. Keen constate sheeting.

or precise phrasing.
re-fin-er-y (ri-fi'no-re) n. pl. see. An industrial plant for purifying

re-finers'y (felf-ne-f) n. pl. -tes. An industrial plant for purifying a crude publishers, pertodicum. In a crude publisher n. pre-fit (felf-ty v. fested, distrian, distr. - yr. To perque and reput for delibitation in ac. - yr. To be made fit again. - yr. (Fift v. fested, distrian, distr. - yr. To perque and reput for the publishers of the proposed of the publishers of the proposed of t

proofs. The partiest placed, indicate, core meaning to send back or me as lines of C, pool that selection of the partiest place of t

b. The resists of such consideration. 4. An imputation of censure or discredit.—reflectionaria discredit.—reflectionaria discredit.—reflective (cf-filek'tity) odf. 1. Of, relating to, produced by, or residing from reflection. 2. Mediative.—reflectively day. reflectively (cf-filek-ity'te) n. pl. -ties. 1. The quality of being reflective 2. Abhility to reflect. 3. Physics. The ratio of the intensity of the total incident on the surface.

re-flec-tom-e-ter (re'flek-tom'l-tor) n. An instrument for measure

ing the reflectance of a surface.

re-flector (rf-flek'tor) n. 1. Something that reflects. 2. A surface that reflects radiation. 3. A reflecting telescope.

re-flex (efficie) oid. [Lit. reflexis, point of selfcexis, at label.—see hundred.] I broad, therein, or best belowed L bed.—see hundred.] I broad the see hundred. I bed on the selfcexis of the

ive mess, reflexivity (reflexivite) n.

refluent (reflexout) adj. [Lat. refluen, pr.part. of refluen, to flow back : re-, back + fluere, to flow.] Flowing back : Manne.

re-form-ism (ri-fôr'miz'om) n. A doctrine or movement of re

reformation (if formiron) is A decrine or movement of reformer-reformates.

Reforms Industrum n. A branch of Judams during from the ribe and the reformation of the r

Lte) n

I-té) n.
refractive index n. Physics. Index of refraction.
refractomerter (réfrisk-tom-t-ter) n. An instrument for mess
uring indices of refraction.
refractor (réfrisk-ton) n. 1. One that refracts. 2. A refracting tile

RODE.

TO THE CONTRIBUTION OF THE CONTRIBUTION

ri-ness n.
re-fraint (n'frish') v. -frained, -frain-ing, -frains. [ME refren
< Ofr. refrener < Lat. refrenare, to restrain : re., back + frene āpat āpay ārcare āfather ēpet ēbe hwwhich lpdt lite îr pier ēpot ē toe ē paw, for ci noise co took is]—r... To hold one-rif buck: NORBERS.—r.r. Ard
for hold back: CURS.——reveniere n.—re-frain's
synthe introduced buck in the control of the

ger www. Spring the (fritarijs-bol) adj. Capable of being reft being right be (fritarijs-bol) adj. Capable of being reft properties of the control of the co

person of the control of the control

age men or same.

(rifrij'er ent) adj. 1. Cooling or freezin ide meal or sa ing fever. —n. 1. A substance, as air, ammonia, wa nig fever. —n. 2. A substance, as air, ammonia, wa nide, for producing refrigeration, either as the work is stringerator or by direct absorption of heat. 2. I ing agent.

as a tilepasses or by discel shorpion of heat. 2.51
mileting sparses of by discel shorpion of heat. 2.51
mileting sparses of the sparses of t

* symm: REFUCE, ASTLUM, SANCTUARY, SHELTER the state of being protected, as from danger <

its the state of being protected, as into angus-to embassys, being being being being being being being refugee (refruge, refuge.) One who fleet, unt. to sluge c.Ofr. refuge, refuge.) One who fleet, on perce-lor refuge, esp. from invasion, opposed, on perce-fulgement (-field) ant. ("All") and [Let refulgement refulgement (-field) ant. ("All") and [Let refulgement being being being being being being being being larger to flash back: no, back - fulgement and and y: suspendoment - definited the refully state of the superior being being being being being being being and yet and the superior being being being being being being state of the superior being being being being being being being state of the superior being being being being being being being state of the superior being being being being being being being state of the superior being being being being being being being being being state of the superior being be

of lends. 2. An amount repaid.—avertunal reason — the furnishment in .

Terfund (rie-fund) vs. -funnded, afund-ing. -fr save. 2. To pay back (a debt) with new bornowing, and issue; with a new bond issue. — the furnishment (rie-fulf-bish) — this hold, -bished sefur bish (rie-fulf-bish) — this hold, -bished sefur bisher sefur bisher.

Bith (clean, bright, or fresh again. and or ferbuing 2. The furnishment (rie-furnishment).

"Tursual (f.t/907221) n. h. n. for the control with the except or relect.

"Tursual (f.t/9002) v. Aussed, -four-ing, -four-ing
Or, refuser v. Vata. *refusers < Lat. refunders, to
Farthern,] — v. h. To decline to do, accept, give, dine to jump (an obstatel). — Used of a horsy of
teeps, allow, or give something — or -four-forrefusel (ref./908) n. [MS – Or; refus. relections of the control o

Shoot ou out the thin the this deut in the shout of the shout item, edible

WEBSTER'S II New Riverside

New Riverside University Dictionary Words that are believed to be registered trackmarks have been checked with anthreduting somes. No investigation has been checked with anthreduting somes. No investigation has been made of commondated randomark rights integrated to the proof. In the contract of the common of the contract registrations are shown with an initial explaint after also disturbed as trackmarks. The inclusion of any word in this Dictionary is not, however, an inclusion of any word in this Dictionary is not, however, and the contract of the contra

Copyright © 1984, 1988 by Houghton Mifflin Company. All rights reserved.

olio part oli thia work may be reproduced or examilitied in any form or by farm glassis, descrease for mechanical lineuter implications of the state of the state

Library of Congress Cataloging in Publication Data Main entry under title:

Webster's II new Riverside university dictionary.

English language—Dictionaries. I. Riverside Publishing Company. II. Title: Webster's two new Riverside university dictionary. II. Title: Webster's 2 new Riverside university dictionary.
 PEI625.W244 1984 / 423 83-3799
 PESRN: 0-395-3957-X (thumb index, trade edition)

0-395-37928-8 [high school edition]

Manufactured in the United States of America

Table of

Lexical and Electro
Preface
Noah Webster and
Explanatory Diagran
Explanatory Notes
A Concise Guide to
Style Guide
Problems in English
Clichés
Redundant Expression
Students' Guide to
Business Letter Styl
Forms of Address :
Abbreviations and 1
Pronunciation Sym
A New Dictionary
Abbreviations
Biographical Names
Geographic Names
Foreign Words and
Table of Measurem
Signs and Symbols